

## **REMARKS**

The Office Action mailed December 16, 2004, has been received and reviewed. Claims 1–6 are pending in the present application. All claims stand rejected. Applicants have amended claims 1, 2, and 3 as previously set forth. Reconsideration of the application in view of the above amendments and the following remarks is respectfully requested.

### **Information Disclosure Statement**

It is stated in the outstanding Office Action that the listing of references in the specification is not a proper information disclosure statement pursuant to 37 C.F.R. § 1.98(b). It is respectfully submitted that all references cited in the specification were properly submitted by way of an Information Disclosure Statement in the parent application hereto (U.S. Application Serial No. 10/002,842). Pursuant to MPEP § 609 I.A.2, a listing of the information has not be resubmitted in the present divisional application. However, applicants intend all such references to be considered with reference to the subject application. If a separate information disclosure statement must be submitted in the present application to ensure such consideration, please advise accordingly.

### **Amendments to the Specification**

Each of paragraphs [0008], [0009], [0013], [0016], [0019], [0030], [0033], [0034], [0036], [0040], [0042], [0043], [0051], and [0058] has been amended as hereinabove set forth to correct inadvertent errors in symbolic designation, typographical errors, and/or minor grammatical errors. It is respectfully submitted that no new matter has been added by way of the specification amendments.

### **35 U.S.C. § 112, Second Paragraph, Rejections**

Claims 1 and 2 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Particularly, claim 1 stands rejected as vague and indefinite in reciting “endogenous” lactoferrin “because it is not clear as to what the term is to encompass.” *Office Action*, page 3, ¶5A. Clarification is requested as to whether “endogenous” is intended to mean the lactoferrin found within the patient or lactoferrin which is native to the patient.

Applicants respectfully submit that the term “endogenous” is intended to describe the lactoferrin that is found within the patient. Such is supported by the as-filed specification at ¶[0023] wherein it is stated that “total endogenous lactoferrin” “comprises lactoferrin derived from endogenous sources, particularly infiltrating leukocytes (i.e., leukocytes, plasma, bile and mucosal secretions).” *Specification*, ¶[0023]. Each of the specified infiltrating leukocytes may be within the patient but not necessarily native thereto.

With regard to claim 2, it is stated in the outstanding Office Action that use of the phrase “serial ten-fold dilutions” is vague and indefinite. It is stated that “it is not clear if applicant means the sample will be diluted 1:10 or 1:? prior to assaying.” *Office Action*, page 3, ¶5B. Claim 2 has been amended herein to indicate that the serial ten-fold dilutions are performed until a measured result indicates a concentration of fecal lactoferrin that provides an optical density reading at 450 nm that is within a linear portion of the standard curve. While this amendment does not provide an exact number of serial dilutions (as such number will vary depending upon the amount of lactoferrin in the sample), it is respectfully submitted that it is within the purview

of one of ordinary skill in the art to determine the number of serial ten-fold dilutions that may be required for a particular sample without undue experimentation.

In view of the above, Applicants respectfully request withdrawal of the 35 U.S.C. § 112, second paragraph, rejection of claims 1 and 2.

### **35 U.S.C. § 102 Rejections**

#### **A.) Applicable Authority**

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdeggal Brothers v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987). “The identical invention must be shown in as complete detail as is contained in the . . . claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 2 USPQ 2d 1913, 1920 (Fed. Cir. 1989). *See also*, MPEP § 2131.

#### **B. Anticipation Rejections Based on the Sugi reference (Sugi et al., *The American Journal of Gastroenterology*, vol. 91, no. 5, pp. 927–934, 1996)**

Claim 6 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Sugi et al., *The American Journal of Gastroenterology*, vol. 91, no. 5, pp. 927–934, 1996 (hereinafter the “Sugi reference”). As the Sugi reference fails to describe, either expressly or inherently, each and every element as set forth in the rejected claim, Applicants respectfully traverse this rejection, as hereinafter set forth.

Independent claim 6, recites a method for monitoring a patient having inflammatory bowel disease. The method of claim 6 comprises obtaining a first fecal sample from the

inflammatory bowel disease patient at a first time, determining the concentration of endogenous lactoferrin in the first fecal sample to obtain a first lactoferrin concentration, obtaining a second fecal sample from the inflammatory bowel disease patient at a second time later than the first time, determining the concentration of endogenous lactoferrin in the second sample to obtain a second lactoferrin concentration, and comparing the first lactoferrin concentration to the second lactoferrin concentration to evaluate any differences therebetween.

By way of contrast, the Sugi reference discloses a method for utilizing fecal lactoferrin as a marker for disease activity in a person having inflammatory bowel disease wherein multiple readings of lactoferrin levels (at 0, 12, 24, 48, 72, and 96 hours after storage at various temperatures) are taken in a single specimen over time as an assessment of protein stability. *See, Sugi reference*, p. 928, col. 2 and FIG. 2. The Sugi reference, however, does not describe, either expressly or inherently, a method for monitoring a patient having inflammatory bowel disease which includes obtaining a first fecal sample from a patient at a first time and obtaining a second fecal sample at a second time later than the first time as recited in the method of independent claim 6. Rather, the method of the Sugi reference describes a method wherein first reading of a fecal sample is taken at a first time and a second reading of the same fecal sample is taken at a second time later than the first time. The Sugi reference lacks any description, express or inherent, of taking multiple fecal samples at different times to monitor a patient having inflammatory bowel disease.

As such, it is respectfully submitted that the Sugi reference fails to describe, either expressly or inherently, each and every element of independent claim 6. Accordingly, claim 6 is not anticipated by the Sugi reference and withdrawal of the 35 U.S.C. §102(b) rejection of this

claim is respectfully requested. Claim 6 is believed to be in condition for allowance and such favorable action is respectfully requested.

### **35 U.S.C. § 103(a) Obviousness Rejections**

#### **A.) Applicable Authority**

The basic requirements of a *prima facie* case of obviousness are summarized in MPEP §2143 through §2143.03. In order “[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success [in combining the references]. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).” MPEP § 2143. Further, in establishing a *prima facie* case of obviousness, the initial burden is placed on the Examiner. “To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references. *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985).” *Id.* See also MPEP §706.02(j) and §2142.

B.) Obviousness Rejection Based on the Uchida reference (U.S. Patent 5,552,292)

Claims 1–3 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the U.S. Patent 5,552,992 to Uchida et al. (hereinafter the “Uchida reference”). As the Uchida reference fails to teach or suggest all the limitations of the rejected claims, Applicants respectfully traverse this rejection, as hereinafter set forth.

Independent claim 1, as amended herein, recites an assay for determining a concentration of total endogenous lactoferrin. The assay of claim 1 comprises obtaining a human fecal sample, diluting the fecal sample, contacting the sample with immobilized polyclonal antibodies to endogenous lactoferrin to create a treated sample, contacting the treated sample with enzyme-linked polyclonal antibodies to create a readable sample, determining the optical density of the readable sample at 450 nm, generating a purified lactoferrin standard curve, and comparing the optical density of the readable sample to the standard curve to determine the concentration of total endogenous lactoferrin in the fecal sample.

By way of contrast, the Uchida reference discloses a method for diagnosing gastrointestinal tract disorders, particularly colorectal cancer, by measurement of the level of lactoferrin “in feces by immunoassay and by measurement of the level of whole-sized lactoferrin by immunoassay utilizing monoclonal antibody.” *Uchida reference* at col. 1, lines 10–19. The Uchida reference extensively evaluates the difference between measuring “whole” lactoferrin (undigested) using a monoclonal based assay. The monoclonal antibody is shown only to bind to undigested “whole” lactoferrin which the Uchida reference further describes as being the useful form for detecting disease in the colon. *See, Uchida reference* at col. 7, lines 3–8 (“it is now found that only the whole-sized lactoferrin . . . in feces should be measured for screening of gastrointestinal tract disorders . . .” (emphasis added)).

It is stated in the Office Action that Uchida references teaches that the method disclosed therein may be used in various types of lactoferrin and directs Applicants to col. 6, lines 58– 61 in support of this proposition. *See, Office Action*, page 6, ¶3. It is respectfully submitted that while the Uchida reference indicates that such various types of lactoferrin were tested, it goes on to state that “only the whole-sized lactoferrin . . . in feces should be measured for screening of gastrointestinal tract disorders . . .” *Uchida reference* at col. 7, lines 3–8 (emphasis added). Thus, the Uchida reference fails to teach or suggest an assay for determining a concentration of total endogenous lactoferrin in a human fecal sample as recited in amended independent claim 1.

Additionally, the Uchida references fails to teach or suggest determining an optical density of the readable sample at 450 nm as recited in amended independent claim 1. Rather, the Uchida reference discloses determining an optical density of a fecal sample at 510/630 nm. *See, Uchida reference* at col. 11, lines 53–55. It is stated in the Office Action that the Uchida reference teaches “that the absorbance measurement is routinely adjusted to optimize the assay” and directs Applicants to col. 5, lines 30–32 in support of this proposition. *Office Action*, page 7, ¶ 1. It is respectfully submitted that the Uchida reference merely states that absorbance is determined at “an optimum wavelength” and then goes on to establish that wavelength at 510/630 nm. *Uchida reference* at col. 5, lines 30–32; col. 11, lines 53–55. The Uchida reference does not teach or suggest any variation of this established optimum.

In view of the above, it is respectfully submitted that the Uchida reference fails to teach or suggest all of the limitations of amended independent claim 1 and, thus, a *prima facie* case of obviousness cannot be established for this claim based upon the Uchida reference. *See, In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). As claim 2 depends from independent claim 1, it is respectfully submitted that a *prima facie* case of obviousness based upon the Uchida

reference cannot be established for this claim for at least the same reasons as amended independent claim 1. *See, In re Fine*, 5 USPQ 2d 1596, 1600 (Fed. Cir. 1988) (a dependent claim is obvious only if the independent claim from which it depends is obvious); *see also*, MPEP § 2143.03. Accordingly, withdrawal of the 35 U.S.C. § 103(a) rejection of claims 1 and 2 is respectfully requested.

Independent claim 3, as amended herein, recites a kit for distinguishing irritable bowel syndrome from inflammatory bowel disease by determining a concentration of total endogenous lactoferrin in a fecal sample from a person to be diagnosed. The kit of amended claim 3 comprises one or more microassay plates, each plate containing immobilized polyclonal antibodies to human lactoferrin, enzyme-linked polyclonal antibody to human lactoferrin, and enzyme substrate for color development.

By way of contrast, the Uchida reference discloses a method for diagnosing gastrointestinal tract disorders, particularly colorectal cancer, by measurement of the level of lactoferrin “in feces by immunoassay and by measurement of the level of whole-sized lactoferrin by immunoassay utilizing monoclonal antibody.” *Uchida reference* at col. 1, lines 10–19. The Uchida reference extensively evaluates the difference between measuring “whole” lactoferrin (undigested) using a monoclonal based assay. The monoclonal antibody is shown only to bind to undigested “whole” lactoferrin which the Uchida reference further describes as being the useful form for detecting disease in the colon. *See, Uchida reference* at col. 7, lines 3–8 (“it is now found that only the whole-sized lactoferrin . . . in feces should be measured for screening of gastrointestinal tract disorders . . .” (emphasis added)).

The Uchida reference does not teach or suggest distinguishing irritable bowel syndrome from inflammatory bowel disease by determining a concentration of total endogenous lactoferrin

in a fecal sample from a person to be diagnosed nor a kit therefore. Accordingly, it is respectfully submitted that the Uchida reference fails to teach or suggest all of the limitations of amended independent claim 3 and, thus, a *prima facie* case of obviousness cannot be established for this claim based upon the Uchida reference. *See, In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). Accordingly, withdrawal of the 35 U.S.C. § 103(a) rejection of claim 3 is respectfully requested.

Each of claims 1–3 is believed to be in condition for allowance and such favorable action is respectfully requested.

C.) Obviousness Rejection Based on the Uchida reference in view of the Foster reference (U.S. Patent 4,444,879)

Claims 4 and 5 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the Uchida reference in view of U.S. Patent 4,444,879 to Foster et al. (hereinafter the “Foster reference”). As the Uchida reference in view of the Foster reference fails to teach or suggest all the limitations of the rejected claims, Applicants respectfully traverse this rejection, as hereinafter set forth.

Claims 4 and 5 each depend from independent claim 3, as discussed hereinabove, and accordingly contains each of the limitations thereof. As previously set forth, the Uchida reference fails to teach or suggest a kit for distinguishing irritable bowel syndrome from inflammatory bowel disease by determining a concentration of total endogenous lactoferrin in a fecal sample from a person to be diagnosed as recited in amended independent claim 3. It is respectfully submitted that the Foster reference does not cure this deficiency of the Uchida reference. Rather, the Foster reference discloses methods and apparatus for immunoassay but makes no mention of determining a concentration of total endogenous lactoferrin.

As such, it is respectfully submitted that the Uchida reference in view of the Foster reference fails to teach or suggest all of the limitations of amended independent claim 3. Thus, a *prima facie* case of obviousness cannot be established for this claim based upon the asserted combination of references. *See, In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). Accordingly, a *prima facie* case of obviousness cannot be established for dependent claims 4 and 5 for at least the above-stated reasons. *See, In re Fine*, 5 USPQ 2d 1596, 1600 (Fed. Cir. 1988) (a dependent claim is obvious only if the independent claim from which it depends is obvious); *see also*, MPEP § 2143.03. Accordingly, withdrawal of the 35 U.S.C. § 103(a) rejection of claims 4 and 5 is respectfully requested.

Each of claims 4 and 5 is believed to be in condition for allowance and such favorable action is respectfully requested.

**CONCLUSION**

Each of claims 1–6 is believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should it be determined that additional issues remain which might be resolved by a telephone conference, the Examiner is respectfully invited to contact Applicant's undersigned attorney.

It is believed that no fee is due in conjunction with the present Amendment. However, if this belief is in error, the Commissioner is hereby authorized to charge any amount required, or credit any overpayment, to Deposit Account No. 19-2112.

Respectfully submitted,



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